REMARKS / ARGUMENTS

Claims 21-47 are currently pending. The present Amendment amends claims 21, 30, 31 and 45. No new matter is added to this case by this Amendment. Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Amendments to the Claims and Support for Amendment

Claims 21 and 45 have been amended to recite that the tablet comprises: "*a lubricating agent in powder form, and a dry mixture of an active substance and excipients including a disintegrating agent and a soluble agent with binding properties*". Support for this amendment can be found, for example, from page 1, line 28 to page 2, line 2; or page 2, lines 10-13 of the application, as originally filed.

Claim 21 has also been amended to replace the term "*adapted to disintegrate in the mouth...*" by "*disintegrating in the mouth...*", which improves clarity.

Claims 21, 31 and 45 have been amended to replace the term "*wherein the active substance is in a form of coated microcrystals or coated microgranules*" by "*wherein the active substance is in a form of microcrystals or microgranules that are uniformly coated with a polymer coating*". Support for this amendment can be found throughout the specification of the application, as originally filed, in particular in the Examples, *e.g.*, page 7, lines 2-6; Table 2; page 8, lines 12-13; Table 4; page 10, line 4; and Table 6.

Dependent claim 30 has been amended to replace the term "*wherein the tablet is adapted to withstand being packaged in...*" by "*wherein the tablet is packaged in...*", which improves clarity.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has maintained the rejection of claim 41 under 35 USC § 112, second paragraph. The Examiner asserts that claim 21 is self-inconsistent as it requires the lubricating agent to be a component of the dry mixture by reciting "a dry mixture of an active substance … and a lubricating agent" and then states that the lubricating agent is only an optional component

of the dry mixture by reciting "and the rest of the lubricating agent, if any, is comprised in the dry mixture". According to the Examiner, it is unclear how the embodiment disclosed in dependent claim 41, namely, that all of the lubricating agent of the tablet is distributed on the outer surface of the tablet, is possible.

As mentioned above, claim 21 has been amended to recite that the tablet comprises:

"*a lubricating agent in powder form, and*

a dry mixture of an active substance and excipients including a disintegrating agent and a soluble agent with binding properties,

wherein more than half of the lubricating agent is distributed on the tablet surface and the rest of the lubricating agent, if any, is comprised in the dry mixture...".

This amendment was made to improve clarity, in particular, to more unambiguously specify that the lubricating agent is not a required component of the dry mixture. The limitation of claim 41 clearly falls within the scope of independent claim 21. The rejection is now moot.

Rejection under 35 U.S.C. § 102

The Examiner has maintained the rejection of claims 21-25, 29-30, 33, 35 and 41 under 35 U.S.C. § 102(b) as being anticipated by U.S. Pat. No. 5,725,880 (hereafter the '880 patent or '880), stating that the arguments submitted in the Response dated October 13, 2008 were not found persuasive.

Applicant respectfully disagrees, and submits that the '880 patent fails to teach every element of the claims, as amended. Elements of the claims that are not taught or even suggested by the '880 patent are listed below.

Active substance in the form of microcrystals or microgranules that are uniformly coated with a polymer coating

Applicant submits that '880 does not teach or even suggest a tablet comprising an active substance which is in the form of microcrystals or microgranules that are uniformly coated with a polymer coating. Indeed, in the present invention, the active substance is uniformly coated

with a polymer coating before being used in the preparation of a compressible tablet. Thus, for instance, in Example 1 of the present application, microcrystals of paracetamol are sprayed with a dispersion of EUDRAGIT E100, EUDRAGIT NE 30 D and colloidal silica in ethanol to obtain microcrystals coated with a polymer coating of the formulation given in Table 2. These coated microcrystals of paracetamol are then used in the preparation of compressible tablets. Similarly, in Example 2, granules of ibuprofen are uniformly coated with a polymer coating comprising ethylcellulose, precipitated silica and hydroxypropylmethylcellulose before being used in the preparation of compressible tablets. In Example 3, granules of paracetamol are coated with ethylcellulose, hydroxypropylmethylcellulose and colloidal silica before being used in the preparation of compressible tablets.

As already mentioned in the Response dated October 13, 2008, the step of wet granulation used in Example 3 of the '880 patent (which was specifically cited by the Examiner) does not result in the active substance (5-aminosalicylic acid) being coated (*i.e.*, being covered with a layer of substance spread over its outer surface). Instead, the wet granulation provides substantially homogeneous granules of the solid ingredients (*i.e.*, 5-aminosalicylic acid, corn starch and polyvinylpyrrolidone). In such granules, the active substance may be considered as being trapped, dispersed, or embedded within a mixture of corn starch and polyvinylpyrrolidone; however the active substance is not uniformly coated with a polymer coating.

Furthermore, in the tablet described in the '880 patent, the active substance is in contact with at least some of the excipients (*i.e.*, corn starch and polyvinylpyrrolidone). In the claimed tablets, the presence of a coating enveloping the active substance implies that the active substance is NOT in direct contact with the tabletting excipients (*e.g.*, disintegrating agent, soluble agent, and lubricating agent). This implicit feature further distinguishes the claimed tablet from the tablet disclosed by the '880 patent.

Tablet disintegrating in the mouth on contact with saliva in less than 30 seconds

Applicant points out that the tablets claimed in the present application "disintegrate in the mouth on contact with saliva in less than 30 seconds", as recited in independent Claim 21. The pharmaceutical preparation for oral administration taught by the '880 patent comprises: "*(a) a*

core containing a medicinal active ingredient; and (b) a press-coated layer comprising an enteric polymer, said layer being provided around the core" (see Col. 2, lines 36-42). The invention of '880 is said to be based on the fact that "*a press-coated layer comprising an enteric polymer starts to dissolve more slowly in the intestine than a film-coated layer comprising the enteric polymer*" (Col. 3, lines 7-10). Furthermore, according to '880, "*during residence of the pharmaceutical preparation in the stomach, the press-coated layer (b) does not dissolve and protects the core (a)*" (Col. 3, lines 19-22). Therefore, the pharmaceutical preparation described in the '880 patent does not dissolve or disintegrate in the mouth.

Tablet disintegrating in the mouth … forming an easy-to-swallow suspension

Applicant submits that disintegration of a tablet recited in independent Claim 21 results in the formation of an easy-to-swallow suspension. The '880 patent does not teach or even suggest such a tablet. Since the press-coated layer of the pharmaceutical preparation described in the '880 patent does not dissolve/disintegrate before discharge from the stomach (Col. 3, lines 23-25), an easy-to-swallow suspension cannot be formed in the mouth.

Tablet having a friability of less than 1%

Applicant submits that the tablets claimed in the present invention "have a friability of less than 1%", as recited in independent Claim 21. The '880 patent does not teach or even suggest such a tablet.

It is axiomatic that a prior art reference must teach every element of a claim in order to anticipate that claim. As demonstrated above, the '880 patent fails to teach every element of the claims rejected by the Examiner. Therefore, the directly compressible tablets of claims 21-25, 29-30, 33, 35 and 41 are not anticipated by the '880 patent, and furthermore, could not be rendered obvious by the '880 patent.

In view of the arguments put forward above, Applicant requests that the rejection under 35 U.S.C. § 102(b) be removed.

Rejection under 35 U.S.C. § 103

The Examiner has maintained the rejection of claims 21-41 under 35 USC § 103(a) as being obvious over Hunter *et al.* (U.S. Pat. No. 6,391,337) in view of Schmitz *et al.* (U.S. Pat. No. 6,079,968), and Valentine (U.S. Pat. No. 4,684,534); and the rejection of claims 31 and 42-47 under 35 USC § 103(a) as being obvious over Hunter *et al.* in view of Schmitz *et al.*

The Examiner has stated that the Hunter *et al.* reference teaches pharmaceutical dosage forms for a rapidly disintegrating tablet, and processes for making this tablet. The Examiner has also stated that the Schmitz *et al.* reference discloses a device that sprays powdered lubricants onto punches and dies of a tablet process and that can be readily retrofitted into existing machinery. The Examiner has taken the position that it would have been obvious to one skilled in the art, at the time the invention was made, to combine the teachings of Hunter *et al.* and Schmitz *et al.* into the objects of the instantly claimed invention. The Examiner cited the Valentine patent, as a teaching reference. Valentine reports that lubricants having a particle size of 44 microns or less are known and desired in the art of manufacturing tablets.

Applicants respectfully disagree, and for reasons set forth below, submits that the Examiner has failed to show that the prior art references teach or suggest all of the claim limitations, as required to support a *prima facie* case of obviousness. Claim limitations that are not taught or suggested by the prior art references, taken alone or in combination, are presented below.

Tablet containing an active substance in the form of microcrystals or microgranules that are uniformly coated with a polymer coating

Applicants respectfully submit that the Examiner has overlooked the limitation which requires that the active substance in the compressible tablet be in the form of microcrystals or microgranules that are uniformly coated with a polymer coating, as recited in independent claim 21. The Examiner has also overlooked the limitation which requires that the method for preparing such a compressible tablet comprises a step of choosing an active substance in the form of microcrystals or microgranules that are uniformly coated with a polymer coating, as

recited in claim 31. The references cited, taken alone or in combination, do no teach or suggest such a feature.

More specifically, the tablet taught by Hunter *et al.* contains acetaminophen (active substance, preferably in granular form), a direct compressible vehicle comprising microcrystalline cellulose (MCC), and a pharmaceutically acceptable lubricant (see abstract). Preferably, the compressible vehicle includes MCC coprocessed with silicon dioxide (see Column 4, line 62 to Column 5, line 1). In this tablet, the active substance is NOT uniformly coated with a polymer coating. Schmitz *et al.* does not describe tablets *per se*. Valentine, which discloses tablets having a harder outer shell and a softer interior containing an active ingredient, does not teach or suggest a tablet containing an active ingredient in the form of microcrystals or microgranules that are uniformly coated with a polymer coating.

Furthermore, in the tablet described by Hunter, the active substance is in contact with the excipients (*i.e.*, microcrystalline cellulose, silicon dioxide, and lubricant). Even if the Hunter tablet was modified according to the teaching of Schmitz and had part or all of the lubricating agent on its surface, the active substance would still be in contact with some of the excipients (*i.e.*, microcrystalline cellulose and silicon dioxide). In contrast, in the claimed tablet, the presence of a coating enveloping the active substance results in the active substance not being in direct contact with any of the tabletting excipients (*e.g.*, disintegrating agent, soluble agent, and lubricating agent). This implicit feature of the claimed tablet is not taught or suggested by any of the references cited, taken alone or in combination.

Tablet disintegrating in the mouth on contact with saliva in less than 30 seconds forming an easy-to-swallow suspension

Applicants submit that the references cited do not teach or suggest a compressible tablet disintegrating in the mouth on contact with saliva in less than 30 seconds forming an easy-to-swallow suspension, as recited in independent claim 21.

Using the United States Pharmacopia (USP) disintegration test (see Col. 5, lines 27-45), Hunter *et al.* have shown that the tablet described in Example 8 has a disintegration time of about

15 seconds (see Figure 3). This test is performed using a disintegrating medium of about 900 mL of an aqueous solution, and a vigorously oscillating apparatus. As known in the art, these conditions are far from those found *in vivo*, and, in particular, the results of a USP disintegration test do not provide a strong correlation with disintegration times in the mouth. Furthermore, the tablet disclosed by Hunter *et al.* is intended for oral administration (see Col. 4, lines 31-33), as well as for "*other uses or locations, such as other body cavities, e.g., periodontal pockets, surgical wounds, vaginally*" (see Col. 14, lines 19-21). However, although the Hunter *et al.* reference describes a rapidly disintegrating tablet, it does not teach or suggest a tablet that disintegrates in the mouth (*i.e.*, an orally dispersible tablet). Adding a lubricant on the surface of the Hunter tablet according to the teaching of Schmitz *et al.* will not make the tablet orodispersible.

Furthermore, the tablet disclosed by Hunter *et al.* is considered as a "convention" rapidly disintegrating tablet for oral administration. Disintegrants included in this kind of tablets ensure that the ultimately prepared compressed solid dosage form has an acceptable disintegration rate in an environment of use (such as the gastrointestinal tract) (see Col. 2, lines 1-4).

In light of the arguments put forward above, Applicants submit that Hunter *et al.*, taken alone or in combination with Schmitz *et al.*, and Valentine, does not teach or suggest all the limitations of the compressible tablet recited in independent claim 21, or of the process for making such a tablet as recited in independent claim 45, and therefore does not render obvious any claims of the instant application.

Furthermore, the Examiner has taken the position that it would have been obvious to one skilled in the art, at the time the invention was made, to combine the teachings of Hunter *et al.* and Schmitz *et al.* into the objects of the instantly claimed invention. In particular, the Examiner has stated that one skilled in the art would have been motivated to combine these teachings "to create an improved process of making pharmaceutical dosage forms that meters out tablet lubricants in a more efficient manner in such a way that minimizes caking of lubricants onto tablet dies" (see page 3 of Office Action mailed 16 June 2005).

Applicants respectfully disagree and submits that one skilled in the art would not have been motivated to combine the teachings of Hunter *et al.* and Schmitz *et al.* to design the claimed process and obtain the claimed tablet. More specifically, as mentioned in the description of the instant application, disintegrating tablets disintegrating rapidly in the mouth often display high friability, therefore requiring special precautions in transport and packaging (see page 1, lines 10-15 of the application as originally filed). Thus, the main aim of the invention was to provide tablets that, among other things, disintegrate rapidly in the mouth and exhibit low friability (see page 1, lines 4-9 and lines 16-22).

The primary goal of using a lubricant according to the teaching of Schmitz et al. is to allow a compressed tablet to easily disengage from a press or die (see Col. 1, lines 45-54). Consequently, one skilled in the art wanting to decrease the friability of the Hunter tablet would have no reason to use the device disclosed by Schmitz *et al.* Furthermore, tablet lubricants, such as magnesium stearate, are known in the art to have a negative influence on tablet hardness, disintegration and dissolution. Therefore, using their general knowledge, those skilled in the art with the goal of decreasing the friability of the Hunter tablet without loss of its disintegrating properties would not be motivated to cover the surface of the tablet with a lubricant.

Applicants further submit that should there have been an incentive to combine the Hunter *et al.* and Schmitz *et al.* references, the combination would not have amounted to the claimed tablet, for at least the reasons set forth above. Accordingly, Applicants respectfully request that the rejection be reconsidered or withdrawn.

New Grounds of Rejection - Rejection under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 21-44 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The Examiner notes that independent claim 21 is self-inconsistent as it requires the lubricating agent to be a component of the dry mixture by reciting "a dry mixture of an active substance.... and a lubricating agent", and then states that the lubricating agent is only an optional component of the dry mixture by reciting "and the rest of the lubricating agent, if any, is comprised in the dry mixture".

As already mentioned above, claim 21 has been amended to more unambiguously specify that the lubricating agent is not a required component of the dry mixture. The rejection is moot.

CONCLUSIONS

For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

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By: 

Robert W. Stevenson
Registration No. 31,064
Customer No. 03000
(215) 567-2010
Attorneys for Applicants

Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.